P.S. Do you have some well-defined auxotrophs from your BTCC 123 strain? We have a few from a prototrophic derivative. How did you test the self-incompatibility of 123? E.M.L.

Department of Genetics
University of Wisconsin

March 26, 1952

Dear Cavalli:

I am replying immediately to your letter of the 21st. After I have had a chance to study your comments, and when some current experiments are concluded, I will write further. To follow your enumeration: (2): I shall have to consult the editors of Genetics, but I am sure that they will assent to a bacteriological paper on F. Our Genetics paper will, I am sure be entirely incomprehensible to many of the very people who should be aware of it (e.g. Hayes). The JGM seems like an excellent suggestion; I trust you will assume major responsibility for it. In view of this development, however, I wonder if we should not reconsider the order of authorship to reflect more accurately the extent of our responsibility. If the Genetics paper were now to be L.,C.,&L., and the JGM C.,L.,&L. it would, I think, tend to give each of us a better sense of propriety in any decisions that have to be made concerning details. Hints as to future developments will be all that are possible. I would leave our Genetics paper in substantially the present form and scope, but will necessarily, I think, mention the Hfr and segregation effects. (3) I think you have an excellent appraisal of Hayes. If he can be persuaded not to rush in where angels fear to tread I think he is bound to contribute in an important way to the field. Do you think that it would be appropriate to include a critique of self-reproducing gametes, etc., in our JGM paper? It might be better to confer with him, so as to give him the opportunity of clarifying his remarks in his own paper. There was so much nonsense in those Nature papers that I was tempted to ignore them altogether. (4) I think now there is now doubt (from our data) that F+ polarity is involved in the linkage aberrations. I wonder, however, if this does not answer an earlier and equally fundamental question: what determines which Mal-S segment is to be eliminated in the formation of the Het persistent diploids? Previously, I had a symmatrical viewpoint, and could not see why in 58-161Het x W-1177 we should usually find Mal- hemizygous diploids, while x W-1177filial it was the W-1177 contribution that was eliminated. I still do not know exactly why or how elimination occurs, but the polarity is at least now explicable: the contribution from the (relatively) F+ parent is the more frequently eliminated. I will stand on earlier evidence that this elimination occurs during or after meiosis, not before. **It will be very difficult to correlate the linkage details without a better understanding of the effects of this elimination. **(See table 6A my CSH ms.) I am beginning to think in terms of relative potency, rather than phenotypic mixtures (although both may participate). W-1678 (a new proline-serine-less) behaves like a stronger F+ to BM and TL lines. This is shown in its near in-fertility with TL- F+. Also, in all combinations with BM and TL F+ and F-, it gives the Sugar - (ie. like 58-161 x W1177) pattern of prototrophs. Similarly with Hfr, which I would rate as the strongest F+. This suggests that in an F+ x F+ cross one of the parents stands as a relative F- compared the other. I am planning some experiments with chemical influences based on the phycological analogies. This scheme explains why BMF- x TLF+ (0 x 2+) is more fertile than BMF+ x TLF- (1+ x 0) or BMF+ x TLF+ (1+ x 2+), and is also in accord with the segregation-elimination business. There is a good deal more to be done along this line. Perhaps the "UV" effect on BMF+ should be checked to see whether it is not actually a light-activation! (4ii). All K-12 F+ agents have behaved alike in my hands, as have recurrent F+ transductions to the same host. (5) Hfr, as you say, does not transduce F+. I am just about to test filials from Hfr x F-. If transducible F+ reappears, it would appear to be fixed or bound in Hfr, but does this mean a different F+ again? I have seen no variation in F+ x Hfr yields. My old attenuated Hfr (no longer Hfr) seems now to transduce F+. Can you confirm? (6) good idea. (7) The Maas strain is very doubtful: it is probably a mutant in the Waksman strain, which does carry F+ and is doubtfully fertile with K-12. Waks, does cross with other coli, but may be self-sterile (thus me). I'll send you W-1305: a M-T-L-F+ which serves as well, (segr. from diploid). (8 i) OK. Suit yourself on authorship. If you would feel easier to commit only yourself, leave the Lederbergs off. Otherwise, we don't mind, (8ii) I hope the paper will be in print in a few days (March issue J. Bact.) and will airmail reprint. We used sm and phage T1; two series of K-12 each. Also, Miss E. McMurtrie has done the same with sm and Brucella abortus.

Sincerely,
(UW Vet. Sci.)

Joshua Lederberg